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J. L. Bulkley M.D.

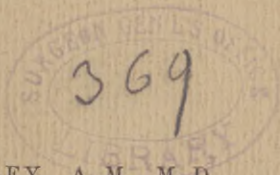
ON THE VALUE OF

FREQUENTLY REPEATED DOSES OF ARSENIC

IN THE TREATMENT OF

BULLOUS DISEASES OF THE SKIN

ESPECIALLY IN CHILDREN



BY

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NEW YORK.

presented by the author

REPRINTED FROM
THE NEW YORK MEDICAL JOURNAL
FOR APRIL 13, 1889

NEW YORK
D. APPLETON AND COMPANY
1889

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BY L. DUNCAN BULKLEY, A. M., M. D.,
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ARSENIC is perhaps the most frequently used and the most commonly abused of all the remedies employed in the treatment of diseases of the skin, and it is safe to say that a large share of all patients with eruptions have this drug administered to them by some one at some time during their course; and yet the experience of every one will testify that it is by no means the specific which could be wished for in these affections when they are taken as a whole. The cause of disappointment in the use of this therapeutic agent will be found unquestionably, as in the case of all therapeutic agents, in the failure to adjust the remedy to the particular diseased state for which it is valuable, and to use it in proper and sufficient doses with, if necessary, such other adjuvants to treatment as may be required. It is needless to add that in this lies the secret of the successful practice of medicine.

* Read before the Section in Dermatology and Syphilography of the American Medical Association, May 10, 1888.

Arsenic is not an indifferent therapeutical agent, and there is no question in regard to its power to influence the skin; but there is also no question but that it is useless, or even harmful, in many of the diseased states to which this organ is liable.

It is not the purpose of the present paper to enter into the general subject of the use and value of arsenic in the treatment of diseases of the skin, nor to dwell on the necessity of an absolutely correct diagnosis and sound therapeutical indications in its administration; this subject was fully discussed by the writer twelve years ago,* and the literature of the subject presented, with also clinical records and illustrations, and later experience has further confirmed the statements there made. The aim of the present communication is to call especial attention to the undoubted and almost specific action of arsenic in one certain form or variety of skin disease, and to place on record a few cases illustrative of the same; also further to show not only the harmlessness but the value of frequently repeated and seemingly large doses of the drug in proper cases, especially in children.

The most notable and striking of all bullous diseases, in which arsenic seems at times to exert almost a specific influence, is pemphigus vulgaris. My attention was first called to the value of efficient doses of arsenic in this affection by the writings of that brilliant, versatile, and indefatigable worker, Mr. Jonathan Hutchinson, who, in 1854, reported a number of cases of pemphigus, some of which had been treated successfully with arsenic; this report was followed by subsequent records of cases by himself and others; and in 1877 the present writer † reviewed the litera-

* "New York Medical Journal," August, 1876, p. 113.

† "American Journal of the Medical Sciences," October, 1877, p. 408.

ture of the subject and reported on five cases of pemphigus treated successfully with arsenic in free doses, in one of which cases the drug had twice appeared to save life. As this latter case was a most important one, demonstrating the specific action of arsenic in pemphigus in an absolute manner, I shall take the liberty of again briefly alluding to it; the other cases here mentioned have been treated since:

CASE I.—Annie S., aged sixteen years, had had an eruption of bullæ, especially on the limbs, coming and going for a year previous to the date of my first seeing her; it had never given great trouble until a few weeks previously, when it increased with severity, the bases of the lesions taking on a diphtheroid character, and she rapidly sinking. When first seen there was every appearance of extreme exhaustion, with rapid and feeble pulse, and death was expected shortly by three physicians who had seen her. The eruption had affected the mouth, and the tongue and buccal cavity, as far as could be seen, were covered with ulcerating lesions, rendering speech and deglutition almost impossible; there were some large and distinct bullæ on the elbows and lower legs, but most of the lesions consisted of ulcerated surfaces, many of them covered with a pultaceous diphtheroid membrane, and some of them were horribly offensive.

All other medicine was stopped, and Fowler's solution was given, well diluted, four times daily, in doses beginning with four drops and increasing by half a drop at a dose until eight drops were taken four times daily. The results surpassed anything I had seen in other cases; within twenty-four hours improvement was very visible, and after three or four days all the lesions assumed a decidedly healthier appearance; a load seemed lifted from the system, the patient was cheerful, could talk easily, and no new bullæ had formed. Within a week or two most of the lesions had healed, no other remedy being used except a little carbolated zinc ointment to a few of the more offensive sores.

Some two months and a half after the first visit she had a relapse, owing to a neglect of the medicine, and once more she was

in bed, prostrated and sinking. Again the eruption yielded to the arsenic alone in full doses, and she kept it at bay for some months, until she sank and finally died from tubercular disease of the lungs, which was aggravated if not induced by her most unsanitary surroundings in a room kept continually damp with laundry work.

CASE II.—Mrs. L., aged twenty-two, had been married five years, and had had several miscarriages before and after the birth of a child, two years and a half previous to the commencement of her eruption; this child was perfectly healthy, and lived four months and a half, dying of some lung difficulty. About three months previous to the date when she was first seen, March 8, 1881, she began to suffer from chills with fever, and an eruption on the forehead, which was followed in three or four days by lesions on the back. The disease increased in intensity until she was shortly confined to the bed, and was more or less helpless up to the time of her admission to Mount Sinai Hospital, on March 3d, where I saw her in consultation with Dr. W. H. Fluhrer.

When seen she was in a pitiable condition; the face was largely covered with crusts, and the arms and legs were also thickly sprinkled with the results of past lesions, in the form of crusted masses, with sharply cut, ulcerated surfaces beneath, scattered among bullæ with more or less purulent contents; there were also a number of lesions on the chest and back. Her temperature on admission was 103° F. and her pulse 104 and weak, and she was emaciated and feeble. From the history and other reasons, syphilis had been suspected, and antisiphilitic treatment had been instituted, under which the eruption had grown worse; she complained of burning pain in all the lesions.

All other treatment was discontinued, and she was given three drops of Fowler's solution, every two hours, well diluted, and a mild carbolic ointment applied to some of the worst sores. The hospital records of March 9th, the next day, show that the eruption had begun to improve at once under the arsenic; and three days later it was recorded that many of the lesions had healed; the dose was then increased to four drops of Fowler's solution every two hours. For some reason, after the eruption

had almost disappeared, she began to get worse, failing in health and strength, and I was asked to see her again on April 8th, the temperature having again run up to 103° at times, with occasional drops to 99°. I found that there had been considerable return of the disease, but the diagnosis of pemphigus was again confirmed, and the arsenic continued in free doses, with attention to the bowels and other details. To be brief, the patient again improved under the arsenic, and was discharged cured on June 17, 1881.

CASE III.—Mr. T., a large, strong man, forty-nine years of age, who had always enjoyed good health, was first seen in consultation with Dr. Klotz and Dr. Scheider, July 28, 1887. He had had pneumonia in January, which was followed very shortly by an eruption of bullæ on the front of the chest; this increased rather slowly, and early in May bullæ existed all over the chest, on the scalp, and within the mouth. After that time the disease developed more rapidly, and he had been confined to bed for three or four weeks previous to the first consultation, spending also part of each day in a water bath, as much relief was obtained thereby.

When first seen much of the surface was covered with the eruption, which exhibited pemphigus lesions in various stages and conditions. The mouth was a mass of raw ulcerative lesions with ragged edges, and the lips were painful to use in any way. The arms, legs, feet, and hands, also the trunk, were the seat of bullous lesions, large and small, with raw surfaces caused by their rupture; the region of the sacrum was entirely bereft of epidermis, as also part of the feet and other portions, so that the suffering was intense.

He was given the liquor sodii arseniatis in doses of two drops, to be increased slowly to ten drops every two hours, in Vichy water, a few drops of laudanum to be added if diarrhœa was produced; a carbolized mouth-wash was prescribed, a calamine-and-zinc lotion applied to some of the inflamed portions, and the raw surfaces were dressed with cotton batting. The effect of the arsenic was seen shortly, and in a week it was recorded that the eruption had improved in every way; some of the sores had healed, and there was much less discomfort; but there had

also been some new development of vesicles, especially on the left upper thigh, where there were dozens of clear, distinct bullæ of small size. The dose of the arsenic had then reached eight drops, but had not been taken as frequently in the twenty-four hours as was desired. One week later there was still improvement in the eruption, and there had been manifest gain in the general condition of the patient, who seemed reasonably comfortable and cheerful. Shortly after this time lung symptoms set in, apparently due to an extension of the disease downward from the mouth, which, however, had greatly improved in condition.

Soon after this the arsenic was discontinued for a day or two, and the change in the character of the eruption and the feelings of the patient was so apparent to every one that it was quickly resumed, and continued to the end. But it seemed finally unable to cope with the disease, for, although it held the eruption in check to a very considerable measure, the patient sank from intestinal complications, with occasional recurrence of his cough, both seemingly from a development of the disease on the mucous surfaces, and finally died on September 10, 1887.

Occasionally during the course of eczema, especially in elderly people, the nature of the process will appear to be changed, and lesions of a pemphigoid character will occur which may prove very distressing. These will continue to be formed in spite of the ordinary treatment employed for eczema, but will be found to yield promptly to the free use of arsenic alone, as in the following two cases:

CASE IV.—Mr. O., aged seventy-seven, was seen in consultation with Dr. J. R. Conway, on February 12, 1884, on account of a very general eczema with which he had been confined to bed for a week. The attack had begun one month previously, and when he was first seen it covered the entire body and limbs, in the form of erythematous and papular eczema; there were no vesicular lesions, but some moist surfaces existed here and there from scratching. The eruption did very well under an acid, magnesia, and iron treatment, together with mild external measures, so that in three weeks he was very comfortable, and

by the end of a month he had been out of doors, and seemed almost well again.

He then became careless in eating, and possibly relaxed treatment too much, and on March 28th it was recorded that he had had severe very general itching, with the production of many large and small erythematous patches, upon which were many grouped vesicles, and three days later there developed on the left wrist a pemphigoid blister, large and tense, nearly an inch in diameter. He was placed on an alkali after eating, and given ten drops of the liquor sodii arseniatis between meals, well diluted. A few days later more of the bullous lesions appeared, one of them three quarters of an inch long, on the front of the right tibia, and other smaller ones elsewhere on the legs. The arsenic drops were increased to twelve, three times daily, and very shortly the production of bullæ ceased. The arsenic was continued until May 10th, and, as he had had no bullæ for some time, they were stopped; but on May 15th they reappeared upon the legs, and he was given the arsenic alone, in ten-drop doses, four times daily, and the bullæ again promptly disappeared. The arsenic was continued for a month longer, and he went to the country apparently well.

In December the eczema recurred, and shortly after the bullæ reappeared, which, however, were again controlled by the arsenic; but his eczema remained more or less troublesome for some months later, although it finally yielded in the spring.

CASE V.—The next case resembled the preceding one very completely, except that the eczema element was less severe and less general; it need, therefore, be but briefly detailed. The patient, Mrs. C., aged seventy-one, was referred to me by Dr. Leaming, February 5, 1877. The eruption had existed some months, and formed eczematous patches over the body and thighs, some of them erythematous and papular, some of them moist. During the course of the eruption pemphigoid blisters developed, mainly on the abdomen, which yielded promptly to the free administration of arsenic.

Arsenic is also found to be of very great service in controlling the bullous eruptions sometimes excited by the in-

ternal use of iodide and bromide salts, especially those of potassium. A single illustration of this will suffice :

CASE VI.—Miss E., aged thirty-five, had been under treatment for syphilis, which was contracted nearly four years previously. As she lived some distance from the city, and neither she nor her family physician could be made to appreciate fully the requirements of the case, her treatment was carried out somewhat irregularly and with interruptions. One year before the occurrence of the eruption to be described, or early in the fourth year of her syphilis, she had a strange attack of partial paralysis, presumably syphilitic, from which she recovered under the treatment of her family physician, who understood her case ; but after this date she had more frequent recurrences of epileptic seizures, to which she had been subject occasionally during the period of her syphilis, though unbeknown to me, and possibly once or twice during previous years. These epileptic seizures had increased during the year previous to my visit to be referred to, and she had been under the care of some irregular physician in another city for this trouble, and had also taken an advertised nostrum for epilepsy. By the latter part of April a bullous eruption appeared on the nose, and then on other portions of the face. This medicine was stopped on April 30th, but her own family physician, thinking the eruption to be syphilitic, had been giving her increasing doses of iodide of potassium, with the effect of daily increasing the eruption until seen by me, May 30, 1880.

When first seen the whole face was covered with a thick, black crust, the results of former lesions, with also much crusting on the scalp. On the chest and back nearly a quarter of the surface was covered with new and old lesions, many being also on the extremities. Here and there could be seen bullæ, rounded on top, up to half an inch in diameter, with apparently clear contents, giving exit to serum and blood when punctured. Some of these were recorded as seated on healthy skin, with almost no surrounding inflammation. Much of the eruption was composed of the crusted and ulcerated surfaces occupied by previous bullæ, and, to render the diagnosis more obscure, they

were largely arranged in circular and serpentine forms. She was extremely exhausted. Pulse, 120; temperature, 101.4° F. in the mouth. The bowels were acting twice daily.

All other medication being discontinued, she was placed upon Fowler's solution, five drops every two hours, to be increased by a portion of a drop if necessary. She was also given a pill containing a third of a grain of opium, with two grains of quinine at bed-time, and locally carbolized oil (1 to 50) to be brushed over the lesions, some of which were very offensive.

The results from the arsenic were even more than could have been expected. Almost immediately the patient began to improve, and three weeks later the eruption had almost entirely vanished. The crusts fell off very shortly after beginning the arsenic, no new bullæ formed, and healing progressed very rapidly. Several months later she was given mild mixed treatment, with a moderate quantity of iodide of potassium, but never again was she troubled with such an eruption.

While arsenic proves of such signal advantage in the conditions already described in adults, its effects in some of the bullous eruptions in children are, if anything, even more marked in proper cases, and if given in efficient doses, as may be judged from the following cases:

CASE VII.—Rosalie B., aged ten years, was sent to me by Dr. J. Ackerman Coles, of Scotch Plains, N. J., May 25, 1887. The child presented a typical herpes iris, and her condition was then as follows: The eruption was confined to the hands and forearms, feet, and lower legs, with a few spots on the thighs and also about the mouth and on the lips, likewise within the buccal cavity. The feet and lower legs were pretty thickly covered with new and old lesions, and on the backs of the hands and wrists some were most typically characteristic, with a single bleb of some size and a circle of vesicles around, seated on a reddened base; in one or two instances there was a second circle outside of this. In some places the blebs were of very considerable size, and were recorded as about an inch in diameter; in other places they had ruptured, and the surface was

either raw or covered with dried membrane or secretions. She suffered very considerably, more especially with the lesions on the lips and mouth, so that she could scarcely talk or take any nourishment.

The history of the case was that in January, four months previous, she had a first attack, which lasted about a week. A second attack came some few weeks later, and was even milder. The present attack had begun three weeks previous to her visit, and had increased steadily until the time she was seen. At the first visit she was given Fowler's solution, with an equal quantity of water, of which she was to take five drops every two hours, increasing the dose gradually to ten drops if necessary and if there were no unpleasant symptoms.

The next day, May 26th, there was already some improvement noted; many of the lesions seemed less inflamed, and the child seemed more comfortable. A little castor-oil was then ordered, as there had been some constipation, and the drops were ordered to be increased. Five days later very marked improvement was noted; the bullæ and vesicles were flattened, and most of the lesions were gone from the mouth, she having used also a lotion of borax, carbolic acid, and honey. A week later the eruption had disappeared, leaving only stains. She was then taking seven drops of the mixture, or three drops and a half of Fowler's solution every two hours.

On two subsequent occasions, when the arsenic was neglected, she had a recurrence of the eruption, which was promptly checked by a return to the frequent doses of the arsenic. The remedy was then taken at longer intervals until finally it was discontinued, and she remained free from eruption.

CASE VIII.—Edward D., aged four years and a half, was brought to me in his mother's arms, October 29, 1887, so severely affected with herpes iris that he could not walk. The eruption began on the foot, four weeks previously, apparently from injury, the toe having been stepped on. The eruption had spread rapidly, with the development of new lesions, until, when first seen, much of the body was the seat of the disease, it being especially severe upon the extremities. The hands and arms were almost covered with old or new lesions, and the feet and

legs so badly affected that they were only wrapped up in bandages, it being impossible to put on shoes or stockings. Much of the eruption consisted of abraded surfaces in various stages of inflammation, some covered with crusts, some raw, and between them, on healthy skin, were some characteristic bullæ of herpes iris, with clustered vesicles around; a new crop had appeared on the backs of the hands and feet the day before the visit, each fresh outburst being preceded by fever. There had been considerable itching, and the child was much pulled down by the disease.

He was given Fowler's solution, diluted one half with water, five drops to be taken every three hours, and a lotion of calamine to be applied freely to the diseased surfaces.

Three days later it was recorded that there had been very great improvement; most of the inflamed surfaces had dried up, but a few new blisters had appeared here and there, with clear contents. The arsenic drops were increased to seven or eight, equaling three or four of Fowler's solution, every three hours, no other treatment being given.

A week later he walked to the office, appearing almost well. There were, however, still a few new blisters developing from time to time, the largest one being on the left wrist, which measured half an inch by a quarter of an inch. It was found that his diet, which had been purposely neglected in order to test the remedy, was very faulty, he taking tea three times daily. These matters were corrected, milk was freely given, and the arsenic continued at six drops, every three hours, as he had shown a little diarrhœa from the drug. The case then progressed satisfactorily to the end, and the mother, seen a year after the last date, reports that all traces of the eruption vanished very shortly, and that it has never reappeared.

CASE IX.—T., a previously healthy boy, aged two years, was seen in consultation with Dr. Packard, January 31, 1885, on account of what then appeared to be a dermatitis, beginning ten days previously on the left foot, from the irritation of rubber boots. It had increased and extended until much of the left foot and ankle were covered with a raw exuding surface, causing much pain. It was learned later, however, that the erup-

tion had begun with blisters like those seen later in the disease. This first attack passed away very shortly under an ointment of oxide of zinc and a calamine lotion, with a little calomel and soda every other morning, and an iron-and-arsenic mixture.

He remained well until the middle of July, when, after a bath in the ocean, an eruption of blisters appeared on the hands and feet and then over much of the body. This passed away in three or four weeks, but returned shortly after on the left leg and buttock; the eruption kept recurring here until the patient was seen again on September 22d, when the hands and face were found to be swollen also, but with no eruption. He was given an alkaline and arsenic mixture with a laxative, and in ten or twelve days the eruption disappeared, and remained absent for a year or more.

When nearly four years old, after bathing daily in the ocean for a month, he had an eruption on the left arm which remained confined there for a month, when it developed on the body and left leg the day before he was next seen, October 2, 1886. There were then found three large bullæ, sharply defined on the left knee, something over an inch in diameter, with perfectly clear contents, with smaller vesico-bullæ on the body, and the remains of others on the left arm; all were seated on a more or less erythematous base, and there was considerable itching before the bullæ developed. As there was evidence of very bad liver action, he was given a mixture of rhubarb and soda with arsenic, and in a week the eruption had pretty much disappeared, but this was followed by a fresh outburst only a week or two later.

These repeated developments of the disease recurred several times until, on November 11, 1887, he was given Fowler's solution, diluted one half, to take from four to eight drops every two or three hours. At this time the eruption was more pemphigoid in character, the bullæ rising quite suddenly from an almost healthy skin, with little or no inflammatory base; the bullæ, some of which were at least half an inch in diameter, were seated on the buttocks, left thigh, and root of the neck. Six days later it was recorded that the lesions had all dried up and that no new ones had appeared, he then taking six drops of

the mixture, or three of Fowler's solution, every three hours. Since that time he has remained free from eruption, and, although he has had disturbances of health requiring attention from time to time, he has never had any return of the bullous disease up to the date of writing.

In looking at these cases, we see that arsenic has proved of signal advantage in several different forms or conditions of bullous eruption, occurring in patients of both sexes and of very diverse ages; the oldest patient was seventy-seven years and the youngest three years of age; four of the patients here mentioned were males and five females. There is seen to be little in common in these cases except the fact that each of them presented bullæ, and that they were mostly of a chronic character, with repeated accessions of eruption until checked by the action of the arsenic. Of the three adults with true pemphigus, two died; but in these instances the drug was commenced very late in the disease, and one of them died, probably from tubercular lung trouble. From the manner in which the remedy controlled the eruption and benefited the patient's condition, from the results in the other cases of pemphigus previously referred to, and from what has been reported by others, there is little doubt but that in efficient doses, with proper adjuvants occasionally, arsenic may be counted on as a specific in pemphigus.

It is especially, however, with regard to its free administration in children, in proper cases, that particular attention is drawn at the present time. Children bear arsenic remarkably well, and, although I have given it freely in a very considerable number of cases, both such as these and in eczema, I have never seen untoward results, or any which caused me uneasiness. As a rule, arsenic acts with them as a purgative before it manifests its other physiological effects, and it may generally be safely given in bullous eruptions in increasing doses; if the disease does not yield, it may

be increased until it purges, then the dose should be slackened to a point where it is perfectly borne.

In many cases, of course, its effect will be more or less increased by the proper use of such other measures of diet and medication as circumstances may indicate; in the first case of a child here mentioned, castor-oil was given, and afterward the hypophosphites were added; and in the last child it was necessary to give occasional doses of calomel, and also an alkali and rhubarb and soda, and finally an iron-and-arsenic tonic; but in each instance it was the arsenic, used independently and in relatively large and frequent doses, which alone checked and controlled the eruption, while in the second case of a child only arsenic was used from first to last.

In regard to the mode of action of the arsenic, it has to be acknowledged that we know little or nothing in reference to the manner in which it operates in controlling the disease. To say that these lesions are neurotic in character and that the arsenic acts through the agency of the nerves, as it is beneficial in chorea and neuralgia, is only bringing the question one point nearer and not answering it completely. Writing upon this subject some time ago, Mr. Hutchinson * uses the following language, which expresses briefly about all we now know of the matter:

“Arsenic does not merely repress the eruption, but remedies the unknown constitutional causes on which that symptom depends, always very much benefiting the general health of the patient. Arsenic does not prevent the liability to subsequent attacks, but such attacks are always much less severe than the original one, and tend, if treated by the same remedy, to diminish in intensity on each successive occasion.”

A single word may be added in regard to the mode of

* Hutchinson, “Medical Times and Gazette,” 1854, vol. i, p. 131.

administration of the arsenic. The preparation used in all these cases was either the arsenite of potassium or the arseniate of sodium in solution. These are undoubtedly the most appropriate preparations, and are those most commonly employed. It is well to prescribe them diluted with a definite quantity of water, both in order that the increasing dose may be more gradually augmented, and that there may be a lessened chance of error in dropping out each dose.

In giving the remedy every two hours it very often or generally comes apart from a meal; it is necessary, therefore, to direct that the dose be administered in a considerable quantity of water—at least a third of a tumblerful. It is often better borne by the stomach when it is given in Vichy water, which is often also otherwise indicated in these bullous affections.

4 EAST THIRTY-SEVENTH STREET.

